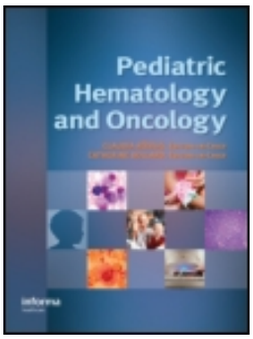

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HEMATOLOGY/TRANSPLANT

The Prevalence and Outcomes of Thrombocytopenia in a Neonatal Intensive Care Unit: A Three-Year Report

Fatih Bolat,[1] Suar Çakı Kılıç,[2] Mehmet Burhan Oflaz,[3] Elif Gülhan,[5] Ali Kaya,[5] Ahmet Sami Güven,[4] Utku Aygüneş,[5] Dilara İçağasıoğlu,[4] and Asım Gültekin[1]

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Neonatal thrombocytopenia is one of the most common hematologic disorders in neonatal intensive care units (NICUs). The purpose of this study was to determine the prevalence of thrombocytopenia and whether thrombocytopenia has an effect on the occurrence of intraventricular hemorrhage (IVH) $\geq$ grade 2 and on mortality rate. This study was carried out retrospectively in neonates admitted to NICU of Cumhuriyet University in Sivas, Turkey, between 2009 and 2012. Among 2218 neonates evaluated, 208 (9.4%) developed thrombocytopenia. The prevalence of IVH $\geq$ grade 2 was more in infants with thrombocytopenia (7.2%) than in those without thrombocytopenia (4.4%), although this was not statistically significant ($P = .08$). In univariate analysis, IVH $\geq$ grade 2 was higher in cases with very severe thrombocytopenia (35.7%, $n = 5$) than in those with mild (2.1%, $n = 2$), moderate (4.7%, $n = 3$), and severe thrombocytopenia (15.2%, $n = 5$) ($P = .04$). Multivariate logistic regression analysis showed that birth weight <1500 g (OR 6.2, 95% CI 3.4–9.8; $P = .0001$), gram-negative sepsis (OR 2.5, 95% CI 1.8–4.2; $P = .01$), very severe thrombocytopenia (OR 1.3, 95% CI 1.1–2.1; $P = .03$), and platelet transfusion $\geq$2 (OR 7.3, 95% CI 4.1–12.1; $P = .001$) were significant risk factors for mortality. The results of our study suggest that outcomes of neonates with thrombocytopenia depend not only on platelet count but also on decreased gestational age or birth weight, prenatal factors, and sepsis.

Keywords intraventricular hemorrhage, mortality, neonatal intensive care unit, prevalence, thrombocytopenia

INTRODUCTION

Neonatal thrombocytopenia is one of the most common hematologic disorders in neonatal intensive care units (NICUs), occurring in up to a quarter of admissions [1]. The prevalence of thrombocytopenia varies depending on gestational age (GA) and degree of illness. Fortunately, the great majority of cases are mild [2]. Given the fact that healthy fetuses at GA $\geq$ 22 weeks and neonates have platelet counts within the

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normal range as adults, the underlying etiology of thrombocytopenia in the newborn may be clarified with perinatal history along with physical examination and peripheral blood samples of the mother and newborn [3].

Few data are available about neonatal thrombocytopenia in NICUs in Turkey, particularly with regard to prevalence and outcome. Numerous studies suggest that neonatal thrombocytopenia is a risk factor for hemorrhage [particularly intraventricular hemorrhage (IVH)], mortality, and adverse neurodevelopmental outcome [1, 4–6]. However, whether these outcomes can be improved by treating affected neonates with platelet transfusion is difficult to assess since there are only a few randomized controlled neonatal trials [2, 7, 8]. Andrew et al. [8] found no reduction in the rate of hemorrhage in neonates randomized to receive transfusions to maintain their platelet counts in the normal range ($>150 \times 10^9$/L) when compared with control neonates with moderate thrombocytopenia ($50–150 \times 10^9$/L), who were not transfused. More recently, a retrospective study about the risks and benefits of transfusions in very premature infants with thrombocytopenia showed that there was no significant difference in the incidence of IVH between the restrictive-transfusion and liberal-transfusion units [9].

The current practice of prescribing platelet transfusion in NICUs is based on limited clinical experimental evidence from differently designed studies, where bias could possibly raise doubt about the results. They do not provide adequate evidence for optimal transfusion practice in neonates [10].

The aim of this study was to establish the prevalence of neonatal thrombocytopenia in our NICU and to determine whether thrombocytopenia has an effect on the occurrence of IVH $\geq$ grade 2 and on mortality rate.

PATIENTS AND METHODS

Cumhuriyet University's NICU is located in Central Anatolia of Turkey, Sivas and serves as a tertiary center and a teaching facility. Approximately 1700 live births occur annually. The NICU has 36 beds and provides intensive care to about 700–800 newborn patients annually. There are 14 intensive care, 8 intermediate care, and 14 rooming-in beds available in the unit. Rooming-in beds are designed to facilitate bonding between the intensive and intermediate care graduates with their mothers before discharge. Medical staffing consists of two full-time neonatologists, four pediatric residents, and 20 neonatal nurses.

We retrospectively collected the data of all neonates who were admitted to the NICU of Medical Faculty of Cumhuriyet University, Sivas, Turkey, between January 2009 and January 2012. Data were obtained from the medical files. The newborns who died or were transferred to another hospital in the first 24 hours of life and who had transient thrombocytopenia were excluded from the analysis. Data were collected by a trained doctor. Data included perinatal history, the infant's status at delivery, and comorbidity [respiratory distress syndrome (RDS), perinatal asphyxia, sepsis, necrotizing enterocolitis, IVH]. This study was approved by the Ethics Committee of the Faculty of Medicine.

Platelet count was performed on ethylenediaminetetraacetate anticoagulated blood using a standard automatic blood cell counter. Diagnosis of thrombocytopenia was based on the finding of a platelet count $<150 \times 10^9$/L. This diagnosis was confirmed with a repeat platelet count within 24 hours along with peripheral blood smear. We classified the patients into four groups on the basis of their lowest recorded platelet count during follow-up: mild ($100–150 \times 10^9$/L), moderate ($50–99 \times 10^9$/L), severe ($30–49 \times 10^9$), and very severe ($<30 \times 10^9$/L). The medical records of 229 neonates

with thrombocytopenia were reevaluated by an experienced hematologist to determine the accuracy and cause of the thrombocytopenia.

Definition

Gestational age of the newborns was determined by early fetal ultrasound and new Ballard score after birth. Newborns were assessed using the Lubchenco scale, according to their weight, height, and head circumference, and those whose measurements were under the 10th percentile were considered as small for GA. Asphyxia was defined as a 5-minute APGAR score < 3, an umbilical arterial blood pH < 7, and/or neurologic manifestations in the immediate postnatal period, including seizures, hypotonia or coma, and evidence of multiorgan system dysfunction [11]. The diagnosis of RDS was made on the basis of clinical, laboratory, and radiological findings. Sepsis was considered in infants who met two or more of the following criteria associated with positive blood culture: fever or hypothermia, tachycardia, tachypnea or apnea, and abnormal white blood cells or increase in band/total neutrophils [12, 13]. The criteria of Bell were used for the diagnosis and staging of necrotizing enterocolitis [14].

Hemorrhage

Bleeding was grouped as IVH, pulmonary, cutaneous, and gastrointestinal bleeding. The diagnosis of IVH was based on the results of cranial ultrasound examinations on day 7 and 21 of life, which were graded according to Papile et al. [15]. Pulmonary bleeding was defined as gross blood suctioned from the endotracheal tube with a chest radiograph consistent with pulmonary hemorrhage. Gastrointestinal bleeding was defined as gross blood in stool after exclusion of necrotizing enterocolitis. Cutaneous bleeding was defined as excessive skin bruising, oozing from venepuncture sites, or hematoma formation. Petechial lesions were not included [16].

Platelet Transfusion Guidelines

Guidelines suggest administering platelet transfusion if the platelet count is 50–100 $\times$ 10^9/L in a newborn with clinical bleeding or within 24 hours before surgery; if the platelet count is 30–50 $\times$ 10^9/L in a clinically unstable newborn or birth weight $<$1500 g; if the platelet count falls below 30 $\times$ 10^9/L in a stable patient [10, 17–19]. However, the guidelines were expert opinions and were not evidence-based; since the decision to transfuse is dependent on the clinician responsible for the infant's medical management at night and weekend shifts, in the present study our unit could not strictly adhere to the guidelines. Due to the retrospective nature of our study, to have optimal results indications of platelet transfusions were classified as prophylaxis or treatment according to hospital records. Treatment was selected as the reason for transfusion if oozing, bruising, or bleeding was recorded in the medical records on that day. If no such items were recorded, prophylaxis was selected. In our hospital, platelets used for transfusion were derived from random donors and were leukocyte depleted. The product was irradiated with 25 Gy for all infants with birth weight $<$1500 g or GA $\leq$ 32 weeks and administered in a volume of 10–15 mL/kg body weight.

Outcomes

The primary outcome was to determine the prevalence of thrombocytopenia. Secondary outcome was whether thrombocytopenia has an effect on the occurrence of IVH $\geq$ grade 2 and on mortality rate.

Data Analysis

Statistical analysis was performed using the SPSS software version 14. The univariate analysis to identify variables was investigated using Chi-square, Fisher exact, Student's

TABLE 1 Demographic Data and Clinical Characteristics of Patients

	Thrombocytopenia (−) ($N = 2010$)	Thrombocytopenia (+) ($N = 208$)	P
Preeclampsia or eclampsia, n (%)	258 (12.8)	58 (27.9)	.02
Fetal distress, n (%)	68 (3.4)	63 (30.3)	.001
Perinatal infection, n (%)	128 (6.4)	48 (23.1)	.01
Antenatal steroids, n (%)	187 (9.3)	85 (40.9)	.001
Multiple births, n (%)	25 (1.2)	7 (3.4)	.9
Caesarean section, n (%)	924 (46)	146 (70.2)	.07
Gender (Female), n (%)	1020 (50.7)	92 (44.2)	.9
Birth weight, mean ± SD	2065 ± 850	1650 ± 280	.001
Gestational age (week), n (%)	34.3 ± 3.3	32.5 ± 2.2	.001
<30	61 (3)	53 (25.5)	.001
30–34	278 (13.8)	79 (38)	.01
$34^{1/7}$–37	722 (35.9)	53 (25.5)	.1
>37	949 (47.2)	23 (11.1)	.001
SGA, n (%)	192 (9.6)	48 (23.1)	.001
APGAR 5 minutes median (min–max)	8 (5–10)	8 (4–10)	.9

Note. SGA = small gestational age.

t test, where appropriate. The variables, which were statistically significant in univariate analysis (the most significant variables in Tables 1 and 2), were entered into multivariate logistic regression model. Stepwise logistic regression analysis was used to determine the effect of thrombocytopenia on IVH ≥ grade 2 and on death. The overall fit of the model was checked with a Hosmer-Lemeshow test. In all tests, the P value < .05 was accepted as significant.

RESULTS

A total of 229 (10%) of 2300 infants had one or more platelet counts $< 150 \times 10^9$/L. Eighty-two of them were excluded from the analysis because of death ($n = 63$) or transfer to another hospital ($n = 19$) within the first 24 hours of life. Twenty-one patients had transient thrombocytopenia, meaning that a repeat count performed within 24 hours was normal. The prevalence was 9.4% (208/2218). Ninety-seven neonates (97/208 = 46.6%) had mild, 64 neonates (64/208 = 30.8%) had moderate, 33 neonates (33/208 = 15.9%) had severe, and 14 neonates (14/208 = 6.7%) had very severe

TABLE 2 The Underlying Causes of 369 Episodes According to Severity of Thrombocytopenia

	Mild ($n = 173$)	Moderate ($n = 115$)	Severe ($n = 44$)	Very severe ($n = 37$)
Preeclampsia or eclampsia	57	21	13	6
Perinatal asphyxia	6	7	5	1
Small gestational age	20	23	2	3
Sepsis	44	32	13	13
Necrotizing enterocolitis	12	6	4	3
Maternal autoimmune diseases (SLE, ITP)	8	5	3	1
Chromosomal disorders	6	2	0	3
Congenital viral infections	2	2	0	2
Unknown/undiagnosed	18	17	4	5

Note. SLE = systemic lupus erythematosus; ITP = immune thrombocytopenia.

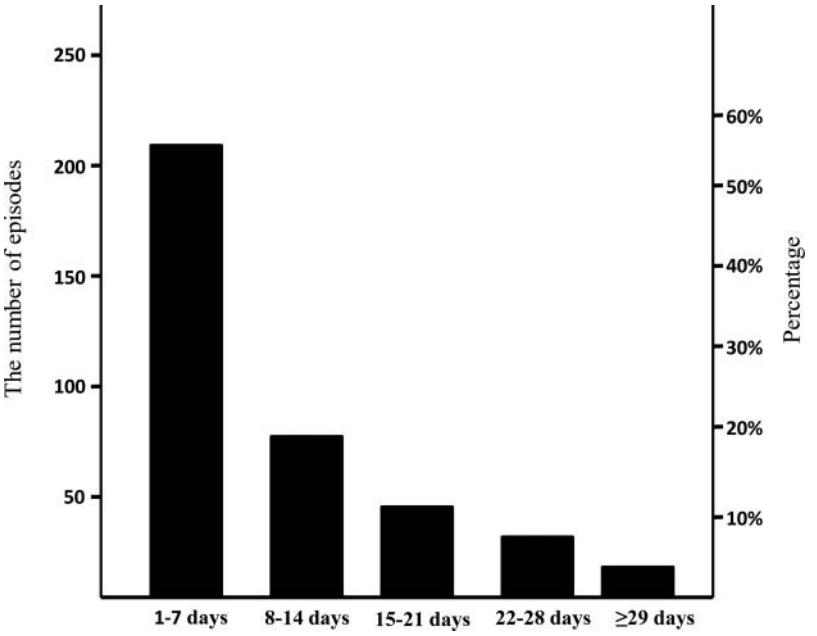

FIGURE 1 Day of onset in neonates developing thrombocytopenia.

thrombocytopenia. In infants born at <34 weeks of gestation, the prevalence of thrombocytopenia was almost sevenfold higher [28% (132/471) vs. 4.4% (76/1747); $P = .001$]. Multiple logistic regression analysis showed that the prenatal factors [(preeclampsia, eclampsia, perinatal infection, fetal distress) (OR 4.4, 95% CI 1.8–9.7; $P = .01$)], preterm birth (<34 weeks) (OR 8.1, 95% CI 6.3–19.7; $P = .001$), and small gestational age (OR 1.5, 95% CI 1.2–5.7; $P = .04$) were associated with the development of thrombocytopenia. However, gender, multiple births, mode of delivery, and APGAR score at 5 minutes were not significant risk factors (Table 1).

During the study period, a total of 369 episodes of thrombocytopenia were detected. Fifty-seven percent of the cases were recognized in the first 7 days after birth. The days of diagnosis of thrombocytopenia are shown in Figure 1. A total of 630 infants were hospitalized in our NICU after the first 48 hours of life. Unfortunately, we did not obtain information about their platelet count at birth.

Predisposing factors for thrombocytopenia were shown in Table 2. Sepsis, particularly gram-negative infections, was the most common cause of neonatal thrombocytopenia. Trisomy 21 was the most common chromosomal syndrome associated with thrombocytopenia. We found that platelet count was significantly correlated with GA and sepsis ($R^2 = .42$ and $R^2 = .36$, respectively, $P < .001$). In multiple linear regression analysis, only GA was significantly correlated with platelet count (expected platelet count = 58,000 + 3200 × GA – 22,000 × prenatal factors – 41,000 × sepsis). Using analysis of variance (ANOVA) to test the model, the result was $F = 46.4$ with $P = .001$, and adjusted $R^2 = .48$, which indicated an appropriate model for prediction of thrombocytopenia.

Hemorrhages

Among 2218 patients, a total of 307 neonates had bleeding that occurred in 61 patients (61/208 = 29.3%) with thrombocytopenia compared with 246 (246/2010 = 12.2%) others who did not have thrombocytopenia ($P = .031$).

TABLE 3 Bleeding Complications in Newborns With and Without Thrombocytopenia

	Thrombocytopenia (−) ($N = 2010$), n (%)	Thrombocytopenia (+) ($N = 208$), n (%)	P
Intraventricular hemorrhage	223 (11.1)	50 (24)	.01
Grade 1	135 (6.7)	35 (16.8)	.02
≥Grade 2	88 (4.4)	15 (7.2)	.08
Pulmonary hemorrhage	13 (0.6)	5 (2.4)	.1
Gastrointestinal hemorrhage	6 (0.3)	3 (1.4)	.5
Cutaneous hemorrhage	4 (0.2)	3 (1.4)	.7

In non-thrombocytopenic group, 13 patients had pulmonary hemorrhages (10 patients < 34 weeks, 2 patients between 34 and 37 weeks, and 1 patient > 37 weeks of GA) whereas there were 5 patients in thrombocytopenic group (4 patients < 34 weeks and 1 patient > 37 weeks of GA). Sixteen preterm infants with pulmonary hemorrhage had RDS, all of whom required assisted ventilation. Fourteen (14/16 = 87.5%) of the infants were treated with surfactant. Only two patients born at term gestation (1 thrombocytopenic, 1 non-thrombocytopenic) had pulmonary hemorrhage due to perinatal asphyxia. They had also received mechanical ventilatory support. Among 18 patients, 5 neonates were administered platelet transfusions after bleeding and all of 5 patients died. Infants with pulmonary hemorrhage who died ($n = 12$) had lower GA compared with those who survived ($n = 6$) (28 ± 2.1 vs. 33 ± 2.3 weeks). The mortality rate of pulmonary hemorrhage was 66.7%.

Pulmonary hemorrhage was more in patients with very severe thrombocytopenia but it was statistically insignificant when compared with cases of mild, moderate, and severe thrombocytopenia. There was also no significant relationship between thrombocytopenia and gastrointestinal, cutaneous, pulmonary hemorrhage, IVH ≥ 2 as shown in Table 3.

In non-thrombocytopenic group, 88 patients had IVH ≥ grade 2 (86 patients < 34 weeks, 2 patients between 34 and 37 weeks of GA) whereas there were 15 patients in thrombocytopenic group (all <34 weeks of GA). IVH ≥ grade 2 developed in three thrombocytopenic patients despite platelet transfusions. Nine neonates had IVH ≥ grade 2 before thrombocytopenia developed. Out of nine, three neonates were administered platelet transfusions.

Intraventricular hemorrhage was the most common form of bleeding and was inversely related to birth weight <1500 g ($P = .03$). Risk of IVH ≥ grade 2 was more in infants with thrombocytopenia (15/208 = 7.2%) than in those without thrombocytopenia (88/2010 = 4.4%), although this was not statistically significant ($P = .08$). In univariate analysis, the prevalence of IVH ≥ grade 2 was higher in cases with very severe thrombocytopenia (35.7%, $n = 5$) when compared with those of mild (2.1%, $n = 2$), moderate (4.7%, $n = 3$), and severe thrombocytopenia (15.2%, $n = 5$) ($P = .04$) (Figure 2). Multivariate stepwise logistic regression analysis showed that birth weight <1500 g (OR 2.7, 95% CI 1.3–8.6; $P = .01$), prenatal factors (OR 3.2, 95% CI 1.3–5.2; $P = .02$), very severe thrombocytopenia (OR 1.4, 95% CI 1.1–6.2; $P = .02$) were predicted factors for the development of IVH ≥ grade 2.

Platelet Transfusion

Out of 111 neonates with moderate, severe, and very severe thrombocytopenia, 42 neonates (37.8%) were administered platelet transfusions, the number of which varied between 1 and 12. The majority of infants (30/42 = 71.4%) were given prophylactic platelet transfusion. All of 14 patients who had platelet count $<30 \times 10^9$/L were transfused. Among those with platelet count between 30 and 49×10^9/L, 20 (60.6%)

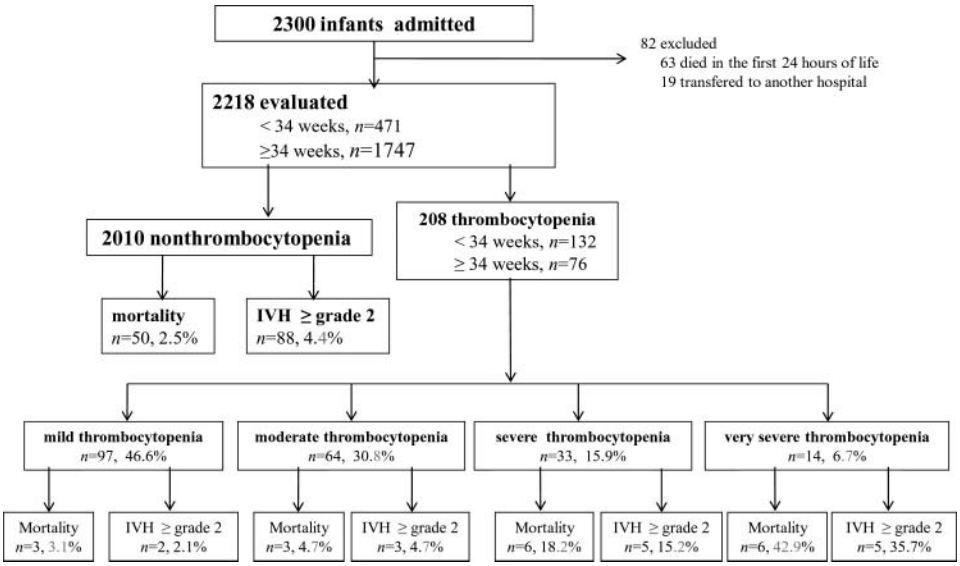

FIGURE 2 Flow diagram of participants in the study.

neonates were given platelet transfusions in clinically unstable conditions. Among those with platelet count between 50 and 99 $\times$ 10^9/L, only eight (12.5%) patients were transfused platelet due to emergency surgery. Transfusion rate was significantly related to the severity of thrombocytopenia and birth weight <1500 g ($P < .01$).

Mortality

Duration of thrombocytopenia in the mild, moderate, severe, and very severe group was 5, 7, 8, and 10 days, respectively. Although it was longer in very severe group, the difference was not significant. Death rates among neonates with mild, moderate, severe, and very severe thrombocytopenia were 3.1%, 4.7%, 18.2%, and 42.9%, respectively. When compared with neonates without thrombocytopenia, death rates among neonates with severe and very severe thrombocytopenia were statistically significant ($P = .04$). The mortality rate of thrombocytopenic patients who received one or more platelet transfusions was more than those who received no platelet transfusions (23.8% vs. 9.4%; $P = .02$). Multivariate stepwise logistic regression analysis showed that birth weight <1500 g (OR 6.2, 95% CI 3.4–9.8; $P = .0001$), gram-negative sepsis (OR 2.5, 95% CI 1.8–4.2; $P = .01$), very severe thrombocytopenia (OR 1.3, 95% CI 1.1–2.1; $P = .03$), and platelet transfusion ≥ 2 (OR 7.3, 95% CI 4.1–12.1; $P = .001$) were significant risk factors for mortality.

DISCUSSION

Our study reveals that thrombocytopenia is a common hematologic problem in patients admitted to NICU. According to our observations, there was a negative correlation between GA and risk of thrombocytopenia. The severity of thrombocytopenia, especially under 30 $\times$ 10^9/L was also correlated with IVH and mortality.

In this study, prevalence of neonatal thrombocytopenia was lower than that was found in previous studies [18, 20, 21]. This may be attributed to some neonates' death in the first 24–48 hours of life and approximately one-third of our patients' hospitalization after 48 hours of life. However, the prevalence of severe thrombocytopenia was similar to some studies [16, 22]. Since the study designs vary widely, incidence

or prevalence of thrombocytopenia, which changes according to the population studied and the platelet threshold used, cannot be known as an exact number [3, 20, 23]. In the studies where thrombocytopenia was defined as platelet count $<150 \times 10^9$/L (as we did in our study), thrombocytopenia has been reported to occur in 18–35% of neonates admitted to NICUs [2, 18].

The disorders associated with neonatal thrombocytopenia are well described in literature [1, 18, 24]. Four kinetic mechanisms have been reported to lead to thrombocytopenia: decreased platelet production, increased platelet destruction, platelet sequestration, and a combination of these processes [3, 25]. The timing and severity of the thrombocytopenia can help in the differential diagnosis. Thrombocytopenia presenting in the first 72 hours of life is usually secondary to placental insufficiency and fetal hypoxia (preeclampsia and fetal intrauterine growth restriction). This form of thrombocytopenia is usually mild or moderate and requires no specific therapy within the first week of life [24, 26, 27]. Thrombocytopenia presenting after 72 hours of life is usually secondary to sepsis, necrotizing enterocolitis, and disseminated intravascular coagulation and is usually more severe and prolonged [2, 26, 28]. Because of the retrospective nature of our study, it is not possible to know the exact mechanisms of thrombocytopenia in our patients. However, based on the finding that 57% of cases were recognized on the first day of life, we observed that there was a strong correlation between perinatal factors and neonatal thrombocytopenia.

Although other causes of thrombocytopenia (thrombosis, alloimmune thrombocytopenia, drug related, severe rhesus disease, etc.) are reported in the literature, none of these etiologies were reported in our patients. However, we cannot comment on alloimmune thrombocytopenia since we are unable to test for alloantigens. Neonatal alloimmune thrombocytopenia might have played a role in the etiopathogenesis of thrombocytopenia in some of our patients.

Bleeding and its management represent common clinical problems in NICUs, particularly in preterm infants because the risk of thrombocytopenia increases progressively as GA at birth declines [4, 16, 20, 26, 29]. Severe organ hemorrhage such as pulmonary, gastrointestinal, and cutaneous hemorrhages are less common, but may require urgent resuscitation and clinical stabilization [7]. In this study, we found an association between IVH $\geq$ grade 2 and very severe thrombocytopenia. Similar observations were reported by Von Lindern et al. [18] and Zisk et al. [30] but this was not confirmed in Baer et al.'s study [16].

In this study, pulmonary hemorrhage that is a rare but well-recognized complication of prematurity and RDS was not significantly associated with thrombocytopenia. Consistent with the literature [31–33], the majority of neonates were preterm and having ventilatory support for RDS, but minority of them was thrombocytopenic. Also platelet transfusion for treatment did not provide any benefit and mortality was high; showing that, pulmonary hemorrhage is a significant indicator of underlying serious disease.

Taking into account that multiple factors contribute to hemorrhage, the findings of our study have to be interpreted with caution because the number of patients with severe thrombocytopenia was small to enable evaluation of significant effect of thrombocytopenia on IVH, pulmonary, gastrointestinal, and cutaneous hemorrhages.

Severe IVH in preterm neonates can result in life-long disabilities or death. Pathogenic mechanisms responsible for IVH are incompletely understood [34]. A number of risk factors including vaginal delivery, low APGAR score, severe RDS, pneumothorax, hypoxia, hypercapnia, seizures, patent ductus arteriosus, thrombocytopenia, and sepsis predispose to the development of IVH [4, 35–37]. It remains unclear whether there was a causal association with thrombocytopenia and IVH. Many of infants with thrombocytopenia are treated with platelet transfusions in an attempt to

decrease the risk or the severity of hemorrhages [16, 26, 38]. However, as the evidence that platelet transfusion improves outcome in neonates with thrombocytopenia is lacking, recent guidelines are more conservative than previous recommendations [7, 38]. As a general rule, platelet transfusion should be given when the degree of thrombocytopenia alone or in combination with other complications result in risk of hemorrhage. A major question for neonatologists regarding the use of platelet transfusion is whether the benefits outweigh the potential complications.

We found that very severe thrombocytopenia and platelet transfusion ≥ 2 were significantly associated with mortality. Several studies have been conducted to determine whether neonatal thrombocytopenia is associated with an increased risk of mortality and adverse neurodevelopmental outcome [23, 39, 40]. However, these studies were mainly retrospective chart reviews [23]. Recently, in another study, a 30% drop in platelet counts, even in the absence of thrombocytopenia, was associated with increased mortality and morbidity in preterm neonates [41]. Therefore, serial measurement of platelets is important for monitoring the patient's condition. It is unclear whether neonatal thrombocytopenia itself directly contributes to adverse outcome or is simply a marker of the severity of precipitating complications [42]. We speculate that this increase in mortality rate is related to the underlying illnesses leading to thrombocytopenia.

CONCLUSION

In this study, we observed that the prevalence of thrombocytopenia in the NICU was inversely proportional to GA. Patients with thrombocytopenia have a wide variety of underlying medical conditions. Very low platelet count is a causal factor in IVH $\geq$ grade 2, but not cutaneous, pulmonary, gastrointestinal bleedings. Outcomes of neonates with thrombocytopenia depend not only on platelet count but also on decreased GA or birth weight, prenatal factors, and sepsis. These results show that in newborn with thrombocytopenia possible risks of platelet transfusion should be carefully balanced against the treatment gains.

We hope that these findings will provide useful information for the practice guidelines and more extensive future studies aiming to reduce the number of platelet transfusions.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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